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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,300	06/15/2001	Lieven De Veylder	2364/300 (C 2681 US)	7567

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,300	DE VEYLDER ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-34 and 41-50* is/are pending in the application.

4a) Of the above claim(s) *2,3,11,12,24-34 and 41-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-10,13-23 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on December 8, 2003 and March 8, 2004 have been entered.

Claims 4 and 35-40 are cancelled.

Claims 1, 5-8, 13-16,18-20 and 50 are currently amended.

Claims 1-3, 5-34 and 41-50 are pending.

Claims 2-3, 11-12, 24-34 and 41-49 are withdrawn from consideration.

Claims 1, 5-10, 13-23 and 50 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claim 1, and claims dependent thereon, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants' arguments filed March 8, 2004 in response to the advisory action mailed January 8, 2004 have been fully considered but they are not persuasive.

Claim 1 as amended is directed to an isolated DNA molecule encoding a cell cycle interacting protein wherein said protein binds to a cyclin-dependent kinase having a PPTALRE cyclin binding motif and wherein said isolated DNA molecule comprises a nucleotide sequence encoding a protein comprising amino acids 96-118 of SEQ ID NO:8, allowing for up to four mismatches. The limitation "a protein comprising amino acids 96-118 of SEQ ID NO:8, allowing for up to four mismatches" does not find support in the specification as originally filed and thus constitutes new matter.

Applicants argue that the limitation does not constitute new matter since this information was present or could be fairly deduced from the specification at page 72, for example, which specifically cites Ferrando et al. (Molecular and Cellular Biology, October 1995, Vol. 15, No.10, pages 5470-5481, Applicants' Exhibit A) (reply pages 2-3).

The rejection is imposed because the limitation "a protein comprising amino acids 96-118 of SEQ ID NO:8, allowing for up to four mismatches" does not find support in the specification as originally filed. See the rejection below under 35 USC 112, first paragraph, for written description.

Claims 1, 5-10, 13-23 and 50 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the

reasons of record set forth in the office action mailed August 5, 2003, and for the reasons set forth below.

Applicants' arguments filed December 8, 2003 have been fully considered but they are not persuasive.

Applicants argue that the amendment of claim 1 to recite that the nucleotide sequence encodes a protein comprising amino acids 96-118 of SEQ ID NO:8, allowing for up to four mismatches, should overcome the reaction because the language recites conserved structural features of the disclosed sequence that are correlated with conserved structural features of the HAL3 sequences (the identical Hal3b and SIS2 yeast sequences) of the prior art, which is known to be functional. Applicants note that the yeast HAL 3 sequences are clearly different from the protein encoded by SEQ ID NO:8 as they differ in 5 amino acids in the region spanning residues 96-118 of SEQ ID NO:8 (alignment, Applicants' IDS Exhibit B). Applicants additionally argue that one skilled in the art could have reasonably derived the 23 amino acid structural feature presently recited in the claims comprising up to four mismatches. (reply pages 12-14)

The amendment of claim 1 to recite that the nucleotide sequence encodes a protein comprising amino acids 96-118 of SEQ ID NO:8, allowing for up to four mismatches, does not overcome the reaction.

First, while the language refers to a conserved structural feature of the disclosed sequence, namely amino acids 96-118 of SEQ ID NO:8, that are correlated with conserved structural features of the HAL3 sequences of the prior art, neither the specification nor the prior art indicates whether this conserved structural feature is correlated with any specific function, or with a function required to practice Applicants'

claimed invention. In this respect the Office notes that part c) of claim 1 requires only that the hybridizing sequence encode a protein comprising amino acids 96-118 of SEQ ID NO:8, and part d) of claim 1 requires only that the nucleotide sequence encode a protein at least 50% identical in general to the amino acid sequence encoded by the nucleotide sequence of part a) or b), such that the only part of SEQ ID NO:8 specifically present in these proteins is the region spanning amino acids 96-118 of SEQ ID NO:8. Yet Ferrando et al. (Molecular and Cellular Biology, October 1995, Vol. 15, No.10, pages 5470-5481, Applicants' Exhibit A) indicates that amino acids outside of the corresponding region in HAL3 are required for HAL3 salt tolerance activity (page 5474 column 1 second full paragraph and page 5473 Figure 1).

Second, the language of currently amended claim 1 is not limited to a conserved structural feature of the disclosed sequence, namely amino acids 96-118 of SEQ ID NO:8. The language of currently amended claim 1 also allows for up to four unspecified mismatches, presumably in the region spanning amino acids 96-118 of SEQ ID NO:8. Neither the specification nor the prior art describe even one such sequence. The specification describes a 201 amino acid sequence of SEQ ID NO:8 obtained from the plant *Arabidopsis thaliana*. The prior art describes a 562 amino acid HAL3 sequence obtained from *Saccharomyces cerevisiae*. As Applicant has noted, the 562 amino acid HAL3 sequence differs from SEQ ID NO:8 in 5 amino acids in the region spanning residues 96-118 of SEQ ID NO:8. Furthermore, the HAL3 sequence differs from SEQ ID NO:8 at 5 specific locations (corresponding to amino acids 107, 108, 109, 110 and 114 of SEQ ID NO:8), by having 5 specific amino acid substitutions (i for V, l for M, v for I, v for I, t for S, respectively) at these specific locations in the region spanning residues 96-

118 of SEQ ID NO:8 (alignment, Applicants' Exhibit B). Neither the specification nor the prior art indicates any other particular combinations of amino acid substitutions that may occur in the region spanning residues 96-118 of SEQ ID NO:8, or where in this region they would be located.

Claims 1, 5-10, 13-23 and 50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to isolated DNA molecules comprising (a) a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:8, (b) a nucleotide sequence of SEQ ID NO:7, nucleotide sequences that hybridize under specified conditions to (a) or (b) wherein the nucleotide sequences encode a protein comprising amino acids 96-118 of SEQ ID NO:8 allowing for up to four mismatches, and nucleotide sequences encoding proteins having an amino acid sequence at least 50% identical to (a) or (b) wherein the nucleotide sequences encode a protein comprising amino acids 96-118 of SEQ ID NO:8 allowing for up to four mismatches. The claims are also drawn to vectors, cells and plants comprising said DNA molecules, and methods of using said DNA molecules for plant transformation or protein production. The claims are additionally drawn to an isolated nucleic acid molecule of at least 15 nucleotides in length hybridizing specifically with a DNA molecule of claim 1.

The specification discloses an isolated nucleic acid of SEQ ID NO:7 obtained from *Arabidopsis thaliana* that encodes a polypeptide having an amino acid sequence of SEQ ID NO:8, said polypeptide interacting with CDC2bAt but not CDC2aAt in a yeast two-hybrid system, and said polypeptide exhibiting amino acid sequence homology to HAL3, a protein encoded by a halotolerance gene of *Saccharomyces cerevisiae* (page 72). The specification also suggests that the claimed nucleic acid may be useful for conferring salt tolerance to a plant or for improving plant growth under saline conditions (pages 72-73). The specification does not disclose a specific function for the polypeptide encoded by SEQ ID NO:7, and the specification does not disclose the effect of transforming a plant or cell with the claimed DNA sequence.

The record also indicates that the region spanning residues 96-118 of SEQ ID NO:8, corresponding to amino acids 376-398 in HAL3 (alignment, Applicants' Exhibit B filed December 8, 2003), is highly conserved, and that the HAL3 sequence differs from SEQ ID NO:8 in 5 amino acids in this region, but the record does not indicate in what way this region is correlated with HAL3 function. The record further indicates that HAL3 sequence differs from SEQ ID NO:8 at 5 specific locations in this region (corresponding to amino acids 107, 108, 109, 110 and 114 of SEQ ID NO:8), by having 5 specific amino acid substitutions (i for V, l for M, v for I, v for I, t for S, respectively) at these specific locations (alignment, Applicants' Exhibit B filed December 8, 2003), but the record does not indicate what other types of amino acid substitutions would be functionally tolerated at these specific locations, or at other locations in the region spanning residues 96-118 of SEQ ID NO:8.

The claimed invention is not enabled because the function of a polypeptide that exhibits homology to HAL3, but that lacks a HAL3 region required for salt tolerance activity, is unpredictable. The function is unpredictable because the record indicates that SEQ ID NO:8 does not possess a domain corresponding to a HAL3 region required for salt tolerance activity (alignment, Applicants' Exhibit B filed December 8, 2003), and because the prior art indicates that the amino acid sequence of HAL3 is not highly homologous to other proteins known to exhibit a salt tolerance activity.

See Ferrando et al. (Molecular and Cellular Biology, October 1995, Vol. 15, No.10, pages 5470-5481, Applicants' Exhibit A), who teach an isolated nucleic acid comprising a nucleotide sequence encoding a 562 amino acid HAL3 sequence obtained from *Saccharomyces cerevisiae* (page 5473 Figure 1). Ferrando et al. also teach that a 58 amino acid acidic domain at the HAL3 carboxy terminus is essential for HAL3 function because deletion at the KpnI site immediately 5' to the acidic domain (the last 71 amino acids) causes loss of salt tolerance activity (page 5474 column 1 second full paragraph and page 5473 Figure 1; page 5475 third paragraph). Ferrando et al. further teach that HAL3 does not fall easily into previously described classes of effectors of transport or homeostasis, since its predicted amino acid sequence shares no significant homology with previously described transporters, signaling molecules or transcription factors (page 5478 column 1 first full paragraph).

The claimed invention is also not enabled because the effect of making amino acid substitutions in a conserved region of a polypeptide is also unpredictable. The effect of making amino acid substitutions in a conserved region of a polypeptide is unpredictable because even a single amino acid substitution in a functional polypeptide

can alter or eliminate its function. See, for example, Rhoads et al. (J. Biol. Chem., November 1998, Vol. 273, No. 46, pages 30750-30756), who teach that mutation of Cys-128 to Ala in an *Arabidopsis* alternative oxidase caused a pronounced overall increase in enzyme activity relative to the wild-type in the presence or absence of pyruvate (page 30753 Figure 3). Mutation of Cys-78 to Ala in the same *Arabidopsis* alternative oxidase resulted in a minimally active enzyme that showed no response to added pyruvate (page 30753 Figure 3).

Claims 1, 5-10, 13-23 and 50 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, for the reasons of record set forth in the office action mailed August 5, 2003.

Claims 1, 5-10, 13-23 and 50 remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, for the reasons of record set forth in the office action mailed August 5, 2003.

Applicants' arguments filed December 8, 2003 have been fully considered but they are not persuasive.

Applicants point out that SEQ ID NO:7 encodes a full length protein, and is not a partial open reading frame. Applicants further argue as above that the amendment of claim 1 to recite a conserved structural feature corresponding to the functional HAL 3 sequence should overcome the rejection (reply pages 15-17).

The rejection is maintained, notwithstanding Applicants' assertion that SEQ ID NO:7 encodes a full length protein, and Applicants' arguments as above that the amendment of claim 1 to recite a conserved structural feature corresponding to the functional HAL 3 sequence should overcome the rejection. Neither Applicants nor the prior art provide any evidence, other than the conservation of sequence itself, that the conserved structural feature corresponding to the functional HAL 3 sequence recited in currently amended claim 1 is sufficient to impart salt tolerance activity on SEQ ID NO:8. Applicants' prior art of record in fact indicates that amino acids outside of the region of HAL3 corresponding to residues 96-118 of SEQ ID NO:8 are required for HAL3 salt tolerance activity (Ferrando et al., Molecular and Cellular Biology, October 1995, Vol. 15, No.10, pages 5470-5481, Applicants' Exhibit A, see page 5474 column 1 second full paragraph and page 5473 Figure 1).

Claim Rejections - 35 USC § 102

Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Ferrando et al. (Molecular and Cellular Biology, October 1995, Vol. 15, No.10, pages 5470-5481, Applicants' Exhibit A).

The claim is drawn to an isolated nucleic acid molecule of at least 15 nucleotides in length hybridizing specifically with a DNA molecule of claim 1.

Ferrando et al. teach an isolated nucleic acid comprising a nucleotide sequence encoding a 562 amino acid HAL3 sequence obtained from *Saccharomyces cerevisiae* (page 5473 Figure 1). While Ferrando et al. do not explicitly teach that the nucleotide sequence encoding HAL3 "hybridizes specifically" with a DNA molecule of claim 1, the

nucleotide sequence encoding HAL3 would necessarily hybridize specifically with a DNA molecule of claim 1, because the DNA of claim 1 comprises a nucleotide sequence encoding a protein comprising amino acids 96-118 of SEQ ID NO:8, allowing for up to four mismatches, which region of SEQ ID NO:8 Applicants have indicated differs in only 5 amino acids from a corresponding region in the HAL3 sequence (alignment, Applicant's Exhibit B). In this regard the Office further notes that claim 5 imposes no specific structural requirements on the claimed isolated nucleic acid molecule except that it is "at least 15 nucleotides in length", and claim 5 imposes no specific functional requirements on the claimed isolated nucleic acid molecule except that it hybridizes "specifically" with a DNA molecule of claim 1.

Remarks

No claim is allowed.

Claims 1, 6-10, 13-23 and 50 are deemed free of the prior art due to the failure of the prior art to teach or suggest a nucleotide sequence of SEQ ID NO:7, or a nucleotide sequence encoding SEQ ID NO: 8, or an isolated nucleic acid comprising a nucleotide sequence encoding a protein comprising amino acids 96-118 of SEQ ID NO:8, allowing for up to four mismatches.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins  6/01/04